STUDY ON DRUG UTILIZATION PATTERN OF DIURETICS AT A TERTIARY CARE TEACHING HOSPITAL

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Submitted by

AARTHI PRIYA.C

261540101

Under the guidance of

Mrs. B.CHITRA, M.Pharm., (Ph.D.)

Assistant Professor, Department Of Pharmacy Practice

COLLEGE OF PHARMACY

SRI RAMAKRISHNA INSTITUTE OF PARAMEDICAL SCIENCES

COIMBATORE- 641044

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CONTENTS

ABBREVIATIONS

ACEI	-`	Angiotensin Converting Enzyme Inhibitors
ADH	-	Anti-Diuretic Hormone
ADR	-	Adverse Drug Reactions
AHF	-	Acute Heart Failure
AKI	-	Acute Kidney Injury
ALoH	-	Ascending loop of Henle
ASH	-	American Society of Hypertension
BP	-	Blood Pressure
BUN	-	Blood Urea Nitrogen
CAD	-	Coronary Artery Disease
CCBs	-	Calcium Channel Blockers
CD	-	Collecting Duct
CDT	-	Combination Diuretic Therapy
CHF	-	Congestive Heart Failure
CKD	-	Chronic Kidney Disease
CO	-	Cardiac Output
CrCl	-	Creatinine Clearance
CRI	-	Chronic Renal Insufficiency
CTDN	-	Chlorthalidone
CVES	-	Cardiovascular Events
CVP	-	Central Venous Pressure
DCT	-	Distal Convoluted Tubule
DDD	-	Defined Daily Dose
DLoH	-	Descending Loop of Henle
DOSE	-	Diuretic Optimization Strategies Evaluation
ECV	-	Extracellular Fluid Volume
ENaC	-	Epithelial Sodium Channels

ESC	-	European Society of Cardiology
ESH	-	European Society of Hypertension
ESR	-	Erythrocyte Sedimentation Rate
eGFR	-	Estimated Glomerular Filtration Rate
HCTZ	-	Hydrochlorthiazide
ICD-10	-	International Classification Of Diseases, 10^{th} Revision
IFR	-	Initial Fluid Resuscitation
INDAP	-	Indapamide
JNC	-	Joint National Committee
MDRD	-	Modified Diet in Renal Disease
MRI	-	Magnetic Resonance Imaging
NDD-CKD	-	Non-Dialysis Dependent Chronic Kidney Disease
NKF	-	National Kidney Foundation
NOD	-	New Onset Diabetes
OATs	-	Organic Anion Transporters
PCT	-	Proximal Convoluted Tubule
RAAS	-	Rennin Angiotensin- Aldosterone System
RBF	-	Renal Blood Flow
RCTs	-	Randomized Clinical Trials
RRF	-	Residual Renal Function
SNS	-	Sympathetic Nervous System
SPIR	-	Spironolactone
TAL	-	Thick Ascending Limb
TD	-	Thiamine Deficiency
TSC	-	Thiazide Sensitive Transporter

ABSTRACT

Diuretics are the mainstay of therapy for a variety of diseases ranging from hypertension to the nephrotic syndrome. The main objective of the study is to assess the utilization pattern of diuretics in a tertiary care hospital in Coimbatore. A prospective observational study was conducted for a period of ten months from november 2016 to august 2017 in general medicine department and intensive care unit of sri ramakrishna hospital, coimbatore. A total of 100 prescriptions were analysed. Through the current study, we could assess the drug utilization pattern of diuretics in ICU and general medicine department. The study report shows male population was higher compared to females. Diabetes mellitus and systemic hypertension were the predominal diagnosis in ICU and general medicine department. ACE inhibitors and diuretics were the most frequently utilized drugs in the study. Among diuretics, frusemide, spironolactone and mannitol were highly utilized in ICU and general Medicine Department. Since diuretic induced electrolyte imbalance were observed during the current study, the clinical pharmacist can be effectively employed to monitor the electrolyte levels to reduce the adverse effects. The current study assessed the major drug interactions which were found to be highly significant. Identifying and monitoring drug interactions has a significant part in forming a standard therapeutic plan will reduce the occurrence of adverse events.

LITERATURE REVIEW

Marouane Boukhris et al (2017)[14] performed a study on the actual place of diuretics in hypertension treatment. Diuretics are widely used, and have several indications in different cardiovascular disorders, particularly in hypertension and heart failure. Despite the large number of available anti-hypertensive drugs, diuretics remained a cornerstone of hypertension treatment. Prescribing diuretics to hypertensive patients seems to be rational and appropriate for a better clinical benefit.

Kristopher R Maday et al (2017)[15] conducted a study on understanding electrolytes, an important diagnostic clue to patient status. Relates the pathophysiological alterations and counter-regulatory pathways linked to electrolyte imbalances. Knowing the concentration of solutes in the blood provides the clinician with meaningful information about the patient's volume status, acid-base status and baseline renal function.

David H Ellison et al (2017)[16] performed a study on time course of loop and thiazide diuretic-induced electrolyte complications. Therapy with a loop or thiazide type diuretic may be associated with a variety of fluid and electrolyte complications, including volume depletion, azotemia, hypokalemia, metabolic alkalosis, hyponatremia, hyperuricemia, and hypomagnesemia. In addition, the potassium-sparing diuretics can induce hyperkalemia and metabolic acidosis, while carbonic anhydrase inhibitors such as acetazolamide can cause hypokalemia and metabolic acidosis.

Donald A Sones et al (2017)[17] performed a study on the effect of thiazide diuretics on plasma volume, body electrolytes, and excretion of aldosterone in hypertension. This study was undertaken in an effort to acquire more information regarding possible mechanisms by which thiazide diuretics reduce the blood pressure of hypertensive patients.

Mathew George et al (2017)[18] performed the study effect of thiazide and loop diuretics on serum magnesium and other electrolytes in cardiac patients. Thiazide and loop diuretics have shown to cause alterations in serum magnesium and other electrolyte levels resulting in fatal complications like ventricular arrhythmias, coronary artery vasospasm or sudden death. By this review we aim at reinforcing the importance of magnesium supplementation and the importance of including serum magnesium among the frequently monitored parameters, in the cardiac department.

Thomas Taylor (2017)[19] studied the monitoring of diuretic use. When thiazide and loop diuretics are used, physicians commonly monitor potassium levels in the blood and prescribe potassium supplements when necessary. Another group of diuretics, known for their "potassium-sparing" effects, includes triamterene, spironolactone and amiloride. Most diuretic drugs are taken once or twice daily. For prescriptions to be used once a day, the diuretic should be taken in the morning. For twice a day use, the diuretic should be taken in the morning and in the afternoon. Because most diuretics can cause urination lasting several hours, each dosage method will usually keep patients from getting up during the night to pass urine.

George C Roush et al (2016)[20] reviewed and updated the study on diuretics for hypertension. This review and update focuses on the clinical features of hydrochlorothiazide, chlorthalidone, indapamide, potassium-sparing inhibitors and aldosterone receptor antagonists, and loop diuretics. Diuretics are the second most commonly prescribed class of antihypertensive medication, and thiazide related diuretics have increased at a rate greater than that of antihypertensive medications as a whole.

L K M De Bruyne (2016)[12] conducted a study on the mechanism and management of diuretic resistance in congestive heart failure. It may be caused by decreased renal function and delayed peak concentrations of loop diuretics

in the tubular fluid, but it can be observed in the presence of pharmacokinetic properties. Removal of excessive fluid is usually achieved by a combination of salt restriction and loop diuretics, but in some cases edema persists despite adequate diuretic therapy. The diuretic resistance can be managed by dose adjustment, intravenous bolus injection or continuous infusion of a loop diuretic, and by combination diuretic therapy, also discontinue NSAID's.

Sonia Gulati (2016)[21] studied on the role of electrolytes in the body. Electrolytes are the minerals found in body fluids that carry an electric charge and are essential to keeping the heart, nerves and muscles functioning properly. It is important to maintain a precise and constant balance of electrolytes to stay healthy. The kidneys play an important role in ensuring that electrolytes remain invariant despite any changes may undergo. An electrolyte imbalance may be caused by loss of body fluids, poor diet, mal absorption, hormonal or endocrine disorders, kidney disease and certain medications like diuretics, antibiotics, corticosteroids and chemotherapy drugs. Treatments include intravenous fluids and dietary changes.

Jaap A.Joles et al (2016)[22] conducted a complicated triangle study of chronic kidney disease, fluid overload and diuretics. Progressive loss of renal function causes reduced sodium filtration and inappropriate suppression of tubular reabsorption that ultimately lead to volume expansion. Various guidelines suggest the use of loop (GFR<30ml/min/1.73m^2) and thiazide diuretics (GFR >30ml/min/1.73m^2) in CKD patients. In conclusion, current study demonstrates that diuretic use is an independent predictor of adverse renal outcomes in NDD-CKD patients causing decline in eGFR and increasing the risk of RRT initiation.

William J Elliott et al (2016)[23] studied loop diuretics are most appropriate for hypertension treatment in chronic kidney disease. Torsemide should be used more frequently today because of its longer duration of action, especially in patients with advanced CKD, its consistent oral bioavailabilty,

and recent generic availability. In contrast, furosemide and other loop diuretics acutely inhibited the Na-K-2Cl cotransporter in the thick ascending limp of the loop of Henle, increasing the fractional excretion of sodium by 20%, largely independent of the level of renal function.

Jozine M et al (2015)[24] studied on the diuretic response in acute heart failure includes pathophysiology, evaluation and therapy. The administration of loop diuretics to achieve decongestion is the cornerstone of therapy for acute heart failure. Unfortunately, impaired response to diuretics is common in these patients and associated with adverse outcomes. The study reveals that the pathophysiological background of diuretic resistance, evaluation and definition of diuretic response, as well as current and future strategies to improve diuretic response in patients with acute heart failure.

Shrenik Doshi et al (2015)[25] studied on the prevalence of thiamine deficiency in heart failure patients on long-term diuretic therapy. It has been shown that loop diuretics cause thiamine deficiency by increasing its urinary loss. Very low thiamine levels (<0.1 ng/ml) was significantly more common in patients with loop diuretics. Use of par-boiled rice in place of polished rice and food fortification with thiamine would be the option to prevent this deficiency. Two-third of study population was thiamine deficient.

Ahmed Hassan Qavi et al (2015)[7] studied on the clinical use of diuretics in heart failure, cirrhosis and nephrotic syndrome. Effective and adequate diuresis can be achieved in patients with cardiac failure, cirrhosis and nephritic syndrome with ideal therapeutic approach of diuretic therapy. Therapy should be directed first to the primary disease mechanism. Each underlying disorder influences the action of the diuretic being administered, Therefore, correct choice of drug is essential for successful management with ascites. These diseases lead to sodium and water retention in patients causing determined effects in their morbidity and mortality. Treatment of ascites in

liver cirrhosis with spironolactone as the primary agent is highlighted with further therapeutic options.

Larry A Allen (2015)[26] conducted a study on the simultaneous use of intravenous fluids and diuretics in patients hospitalized with heart failure. The delivery of IV fluids among congested patients with heart failure reflects variations in the culture of care. Pointing out the frequency with which U.S. hospitals give IV fluid and loop diuretics to patients presenting with worsening heart failure suggests a way forward to our goal of improving acute care.

Jeffrey Freund et al (2015)[27] performed a study on the risk of gout with the use of thiazide diuretics. Thiazide diuretics may be used in most patients with hypertension who have only minimally increased risk of gout. Usual doses of thiazides (less than 25 mg) are not associated with an increased risk of gout, although doses of 25 mg or greater are. The risk of gout with hydrochlorothiazide and chlorthalidone is similar. Thiazides may be used in patients with asymptomatic hyperuricemia because they are not associated with an increased risk of gout in these patients.

Jainaf Anchiya et al (2014)[27] studied on the utilization pattern of anti-hypertensive medications on out-patients and inpatients in a tertiary care teaching hospital: a cross sectional study.11.4% were prescribed with diuretics. The clinical pharmacists can be effectively employed for rationality use of medication in hypotensive population on a routine basis. Diuretics prescribed in single therapy, dual therapy and triple therapy with ACE inhibitors, calcium channel blockers and beta blockers. The diuretics prescribed in this study was hydrochlorthiazide and furosemide. ACE inhibitors were most frequently utilized and amlodipine was the highest consumed drug in this study.

Mabel Bolos (2014)[28] performed a clinical trial to compare the effectiveness of diuretics in hemodialysis patients with residual renal function. When starting the haemodialysis, the patient holds the residual renal function which is lost over time. To preserve the residual renal function, the patient is treated with diuretics loops and thiazide diuretics. The effect of this treatment is lost when renal function worsens. The treatment with frusemide and hydrochlorothiazide in hemodialysis patients with RRF could to decrease in weight gain between hemodialysis sessions, to increase urine volume, to decrease the ultrafiltration in haemodialysis sessions.

Fidelia Bode – Thomas (2014)[29] performed a study on serum electrolytes in children on chronic diuretic therapy for heart failure. They interfere with the reabsorption of sodium, potassium, and chloride ions and also calcium and magnesium ions and may deplete the blood levels of these electrolytes. They may also result in acidosis as a result of the body's attempt to compensate for hypokalemia by exchanging hydrogen for potassium ions at the distal convoluted tubule.

Spyridon Arampatzis et al (2013)[30] studied on the impact of diuretic therapy associated electrolyte disorders present on admission to the emergency department. Diuretics are among the most commonly prescribed medication, and due to their mechanisms of action, electrolyte disorders are common side effects of their use. The study also reveals the association between diuretics being taken and the prevalence of electrolyte disorders on admission as well as the impact of electrolyte disorders on patient outcome such as hyponatremia, hypernatremia, hypokalemia, hyperkalemia.

Annie Claire et al (2013)[31] conducted a study on fluid management and use of diuretics in acute kidney injury. Critically ill adult patients at risk for or with acute kidney injury require careful attention to their hemodynamic status because hypotension and hypovolemia may contribute to or worsen kidney

injury. The efficacy of these procedures in critically ill , patients need to be confirmed with randomized controlled trials. This review focuses on early volume resuscitation, overall fluid management, and use of diuretics in critically ill adult patients at risk for or with acute kidney injury and their effect on mortality and kidney function in this setting.

Jyotsna Rimal et al (2013)[32] performed a study on acute hyperkalemia and hyponatremia following intraoperative mannitol administration. Intravenous mannitol may lead to electrolyte disturbances involving sodium and potassium and resulting in cardiac dysfunction. This report demonstrates that when mannitol is given during intracranial surgery it can cause large increase potassium ion concentration and decrease in sodium ion concentration in the absence of any other possible causes. Intraoperative checks of serum electrolyte levels, arterial blood gas analysis and electrocardiogram monitoring could be recommended to be done routinely when using mannitol.

Mishra Snigha et al (2013)[8] studied on the review on recent advances in a modern day treatment diuretic therapy. Diuretics continued to be a good modern day option for lowering blood pressure, edema, congestive heart failure, cirrhosis, autism, toxemia. For the majority of patients, diuretics can be used as first line therapy. The choice of drugs to initiate therapy for the management of hypertension remains contentious and diuretics are central to its controversy. Thiazides were the first tolerated efficient anti-hypertensive drugs that significantly reduces cardiovascular system morbidity and mortality in placebo-controlled clinical studies.

Sharon J Nessim et al (2013)[33] conducted a case- control study on the concurrent use of diuretics, angiotensin converting enzyme inhibitors, and angiotensin receptor blockers with non-steroidal anti-inflammatory drugs and risk of acute kidney injury. The risk was greatest at the start of treatment.

Although antihypertensive drugs have cardiovascular benefits, vigilance may be warranted when they are used concurrently with NSAIDs.

OP Kalra et al (2012)[34] performed the study on rational use of diuretics and pathophysiology of edema. High doses of loop diuretics can increase urine production in patients with chronic renal failure. Continuous infusion of loop diuretics offer potential benefits compared with intermittent bolus dosing. Treatment of diuretic resistance may require high doses of loop diuretics, a combination of loop and thiazide diuretics, or loop diuretics with albumin infusions. The level of glomerular filtration rate and need for reduction in ECF volume dictates the choice of diuretic agent.

Michael Mc Evoy (2011)[35] assessed the relationship of high blood pressure, dehydration and electrolyte imbalance. There is an intrinsic link between chronic hypertension, renal failure, dehydration and a deficiency of certain electrolyte minerals. Water and electrolytes are absolutely two of the most critical components of normal, physiological function. Without a correct balance of fluid and electrolytes, the cells of our body lack the essential electrical conductivity necessary for cellular energy production. When fluid retention accompanies hypertension, it is a primary indicator of intracellular fluid loss, and an accumulation of extracellular tissue fluids.

Robert F Reilly et al (2010)[36] studied the use of thiazide diuretics in hypertension and nephrolithiasis. Future studies examining the role of low-dose thiazides on calcium-containing kidney stone recurrence would be of interest. In hypertension, chlorthalidone (12.5 to 30 mg daily) may the best option for initial therapy, with indapamide (1.5 mg daily) being a valuable alternative for older patients. When adding a thiazide to other drug classes, indapamide (2.5 mg daily) has clear value in hypertensive patients who have had a stroke, and HCTZ (12.5 to 25 mg daily) has a safe track record in several groups.

Allan S et al (2010)[37] performed a study on thiazide diuretics and primary hyperparathyroidism. This study suggests that thiazide diuretics can be given safely to patients with primary hyperparathyroidism. In fact, thiazide-induced reduction in hypercalciuria might benefit patients by lowering risk for calcium kidney stone formation. However, serum calcium levels still should be monitored periodically, because they occasionally will increase further when patients with primary hyperparathyroidism receive thiazide diuretics.

SCOPE OF THE STUDY

Diuretics are the mainstay of therapy for a variety of diseases ranging from hypertension to the nephrotic syndrome. In the aging population, the number of patients treated with diuretics for different indication is increasing. Various classes of diuretics exist, each having a unique mode of action. Diuretic therapy itself and disorders of serum sodium and potassium were risk factors for an adverse outcome. The seventh report of the joint national committee reports that 35% to 40% mean reductions in stroke incidence, 20% to 25% in myocardial infarction, and more that 50% in heart failure[38]. It is estimated that in patients with stage I hypertension and additional cardiovascular risk factors, achieving a sustained 12-mm Hg decrease in systolic blood pressure for 10 years will prevent 1 death for every 11 patients treated. Diuretics are very effective in preventing stroke and coronary heart diseases. Loop diuretics are an integral part of heart failure management[46]. Thiazide diuretics were the first tolerated efficient anti-hypertensive drugs that significantly reduced cardiovascular morbidity and mortality in placebo-controlled studies. Loop diuretics cause thiamine deficiency by increasing urinary loss. 67% of study population had thiamine deficiency (whole blood free thiamine level <0.7 ng/ml).patients on diuretics had significantly lower thiamine level when patients on loop diuretics[25].

In the clinical setting, measurement of the electrolytes, or solutes, in the blood is one of the most frequently ordered laboratory tests. Interpretation of the results provides information about volume status, acid-base status, and baseline renal function. Evaluating any disequilibrium in electrolytes can be challenging and requires an understanding of the pathophysiology of diseases that can cause electrolyte imbalances; the counter-regulatory pathways of the body to correct the imbalance[21].

Loop diuretics were an independent risk factor for hypernatremia and hypokalemia, while thiazide diuretics were associated with the presence of hyponatremia and hypokalemia. Studies investigating diuretic therapy induced electrolyte disorders have mainly focused on the effects of thiazide diuretics. In a randomized trial in hypertensive patients, serum potassium levels were significantly

lower in patients treated with thiazide diuretics. The patients who did not receive potassium supplements developed marked hyperkalemia with potassium levels below 3.0 mmol /L[32].

The incidence of nephrotic syndrome is about 3 new cases per 1,00,000 each year in adults. In a study assessing the long-term effect of metalozone in patients with nephrotic syndrome, loss of edema and improved control of BP was observed. Moreover addition of furosemide enhanced diuresis. Recent evidence from animal studies and clinical investigations have thrown new light on mechanisms that contribute to diuretic resistance in models or patients with chronic renal insufficiency or the nephrotic syndrome. In a study of diuretic response in heart failure patients, very low thiamine levels (<0.1 ng/ml) was significantly more common in patients on loop diuretics[32].

Diuretic use in body building reviews that diuretics increase the risk of NOD (New Onset Diabetes). In a network meta- analysis of 221 clinical trials, ACE Inhibitors, angiotensin receptor blockers, calcium channel blockers, and placebo were associated with a significantly lesser risk of new onset diabetes compared with diuretics. Studies on new insights into diuretic use in patients with chronic renal disease reports that an observational study of 125 patients with end stage renal disease treated by peritoneal dialysis showed that sodium and fluid removal by peritoneal dialysis were powerful predictors of a good survival. In contrast, a controlled clinical trial of the effects of furosemide in patients treated with continous ambulatory peritoneal dialysis showed no benefit of regular diuretic therapy in delaying the loss of residual renal function. Thus, optimal dialysis, rather than loop diuretic therapy, is the best treatment for these patients[33].

Understanding these disturbances can improve patient care, be cost-effective, prevent complications from primary disease, and ultimately reduce mortality and morbidity. As the adverse effects are increasing due to diuretic therapy, this study was planned to analyze various aspects of diuretics[30].

OBJECTIVES

The main objectives of the study are,

- To study the utilization pattern of diuretics in the general medicine department and intensive care unit.
- To monitor and detect the electrolyte disorders with diuretic therapy.
- To identify the drug interactions and their severity.

PLAN OF THE WORK

The entire study was planned to be carried out for a period of ten months from november 2016 - august 2017. The proposed study was designed in four different phases to achieve the objectives.

PHASE 1:

≫ Literature review

≫ Preparation of protocol

≫ Obtaining consent from the hospital authorities

PHASE II:

≫ Preparation of patient consent form

≫ Designing of structured data entry format

≫ Data collection

≫ Documentation of collected data using the data entry format

PHASE III:

≫ Analysis of all collected data

≫ Graphical representation of the data

≫ Interpretation of the data

PHASE IV:

≫ Preparation of the project report and submission to the study department.

METHODOLOGY

STUDY SITE

The proposed work entitled **"Study on drug utilization pattern of diuretics at a tertiary care teaching hospital"** was carried out in a 750 bedded multi- speciality institution, one of the largest hospitals in coimbatore. The various specialties include general medicine, anesthesiology, orthopedics, radiology, nephrology, pulmonology and critical care, cardiology and cardiothoracic surgery, microbiology, pathology and hematology, laproscopic surgery, dental and maxillofacial surgery, neurology, ophthalmology, physical medicine and rehabilitation, diabetology, surgical gastro enterology, oncology. The hospital is also equipped with the modern diagnostic facilities like CT scan, MRI scan, PET scan, ultrasound sonography, digital subtraction angiography, ECG, treadmill, colour Doppler. The hospital also has twelve hi-tech operation theatres, intensive care unit, intensive cardiac unit, intensive pulmonary care unit, catheterization, balloon valvoplasty, coronary stenting, kidney transplantation units like hemodialysis machines and an assisted reproductive technology centre.

DEPARTMENT SELECTED FOR STUDY

The department selected for the study was intensive care unit and general medicine department. The reason for selection of this department was to analyze the indication and utilization of diuretics in different disease conditions. It was also identified that, the intensive care unit and general medicine department has got potential to use many classes of diuretic drugs. Pharmacy practice department provide services to the department and a good co-operation from medical team added up to the reason for selecting this department for conducting the study.

CONSENT FROM HOSPITAL AUTHORITIES

The protocol of the study that includes the scope of the study, objectives, methodology, etc was submitted to the dean of the hospital. The protocol was presented to the members of ethical hospital committee and the approval to carry out the study was obtained. The authorization from the dean to carry out the study was procured through his letter and the same is attached for reference in the **[Annexure 1].** The study was conducted with the expert guidance of senior and junior physicians of the study department. The author was allowed to utilize the hospital facilities to make a follow up of the cases, in the selected department. The entire health care professionals were well informed through dean's official circular.

LITERATURE SURVEY

Literature survey was carried out regarding the different aspects that should be considered while doing a study based on diuretic therapy. These include use of diuretics in patients, class of diuretics used, diuretic- associated electrolyte disorders, and the therapeutic guidelines to overcome the electrolyte abnormalities. The literature supporting the study was gathered from various journals.

STUDY SITE	**:**	Intensive care unit and General medicine department
STUDY DESIGN	**:**	Prospective observational study.
STUDY DURATION	**:**	10 months (from november 2016- august 2017)
SAMPLE SIZE	**:**	100 patients

PATIENT SELECTION:

Inclusion criteria:

All the in-patients receiving diuretic therapy and patients willing to participate are included in the study.

Exclusion criteria:

Out-patients, pregnant women, pediatric patients and those not willing to participate in the study are excluded from the study.

PATIENT CONSENT FORM

A patient consent form has been prepared and written consent was obtained from the patient attenders. The format contains details like name, address, date, place, provision for signature of the patient or caregivers, investigator and supervisor. The same is given in **[Annexure No. 2].**

DATA ENTRY FORMAT

A specially designed data entry format was used to enter all patient's details like patient name, age, sex, date of admission, date of discharge, reason for admission, past medical history, medication history, social history, type of diuretic prescribed, dose, duration, electrolyte disorders, and vital signs like BP, pulse and temperature. Provision is given in the format to enter the laboratory investigations like blood counts, blood sugar levels, liver function tests, renal function tests, urine examination, diagnosis, drugs prescribed, drug interactions, adverse drug reaction monitoring and interventions. Lipid profile were also noted down. The same is given in the **[Annexure No. 3]** for reference.

METHODS AND MATERIALS

The data was collected during the regular ward round participation in the general medicine department and ICU. Standard data entry format was used to enter all the patient details collected during ward rounds. Patient information's such as their social history, body mass index, laboratory investigations, sugar levels, blood counts, BP, electrolyte levels, uric acid levels and the drugs prescribed for the patients are

noted down from the patient's record in the data entry format. The prescriptions were individually screened to assess the prevalence of diuretic therapy and associated electrolyte disorders. Micromedex drug data base was used to identify the drug –drug interactions and their severity in the prescriptions.

REPORT SUBMISSION

The reports on the study results were prepared and the same was submitted to the study department.

TABLE NO.1

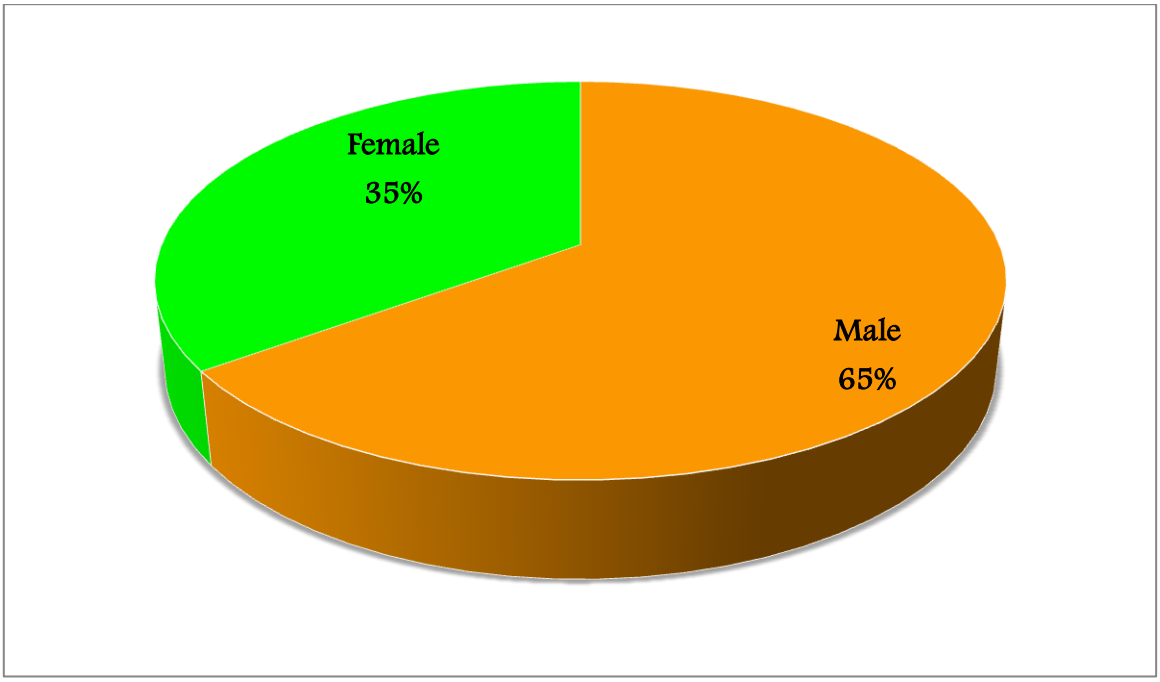
GENDER CATEGORIZATION

(n=100)

Sex	No. of patients	Percentage (%)
Male	65	65
Female	35	35

FIGURE NO.1

AGE CATEGORIZATION



The study results shows that 65% of the patients were male and 35% were female.

TABLE NO. 2

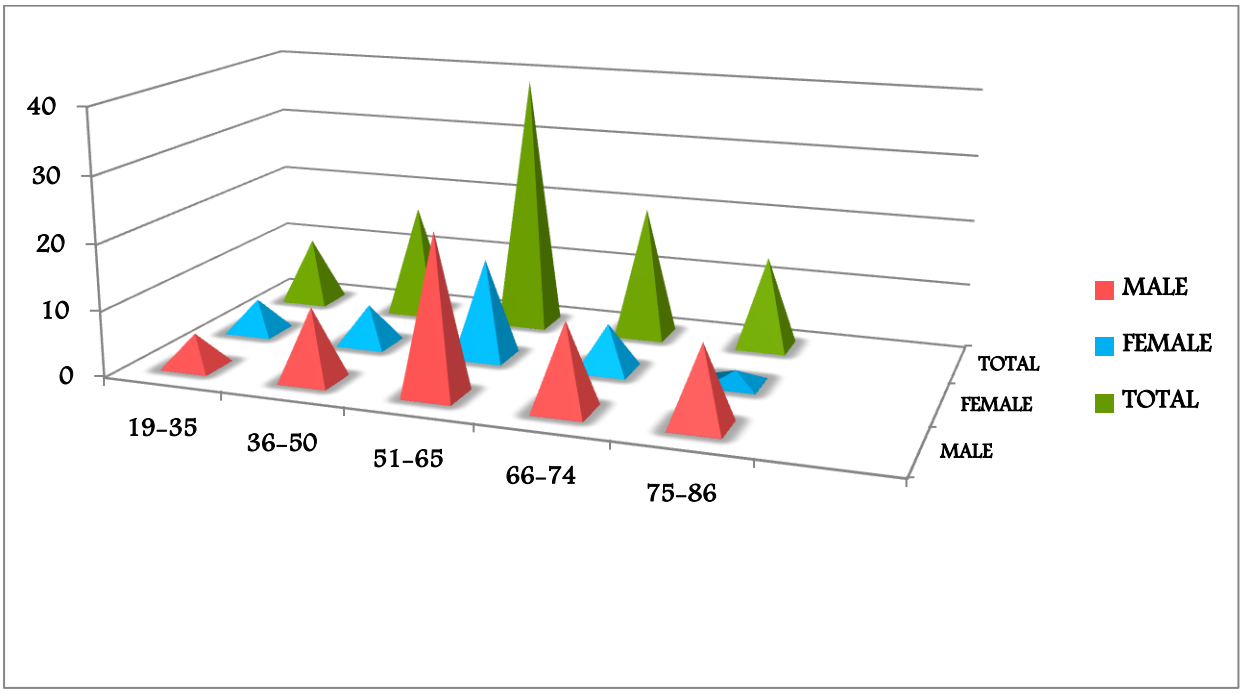
AGE CATEGORIZATION

(n=100)

Age	Male	Female	Total	Percentage(%)
(19-35)	5	5	10	10
(36-50)	11	15	26	26
(51-65)	24	6	30	30
(66-74)	13	7	20	20
(75-86)	12	2	14	14

FIGURE NO.2

AGE CATEGORIZATION



Age distribution of the patients were analyzed and it was found that 10% of the prescriptions were in the age group of 19-35 years, followed by 26% in the age group of 36-50 years, 30% in the age group of 51-65 years, 20% in the age group of 66-74 years and 14% in the age group of 75-86 years.

TABLE NO.3

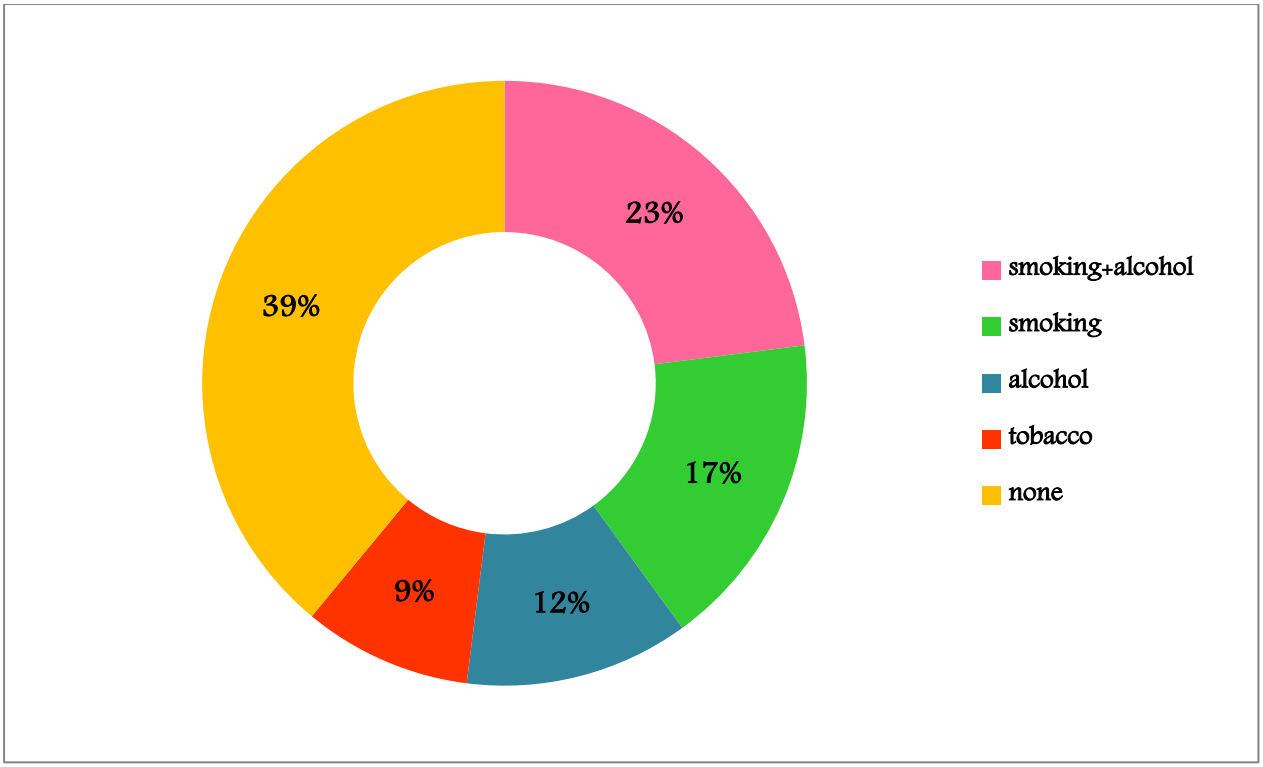
SOCIAL HISTORY

(n=100)

S.No	Category	No. of patients	Percentage %
1	Smoking+ Alcohol	23	23
2	Smoking	17	17
3	Alcohol	12	12
4	Tobacco	9	9
5	None	39	39

FIGURE NO.3

SOCIAL HISTORY



The social history of the patients reveals that 23% of study population have the habit of both smoking and alcohol consuming, 17% were found to be smokers, 12% were alcoholics and 9% were tobacco consuming.

TABLE NO.4

DIAGNOSIS OBSERVED IN THE STUDY POPULATION

(n =100)

No.	Diagnosis	No. of patients	Percentage(%)
1	Diabetes Mellitus	35	27
2	Systemic Hypertension	30	23
3	CAD	12	9.3
4	RTA	7	5.4
5	IHD	6	4.6
6	Bronchial Asthma	4	3.1
7	CLD	3	2.3
8	Stroke	3	2.3
9	ARF	2	1.6
10	CHF	2	1.6
11	Suicidal	2	1.6
12	Ulcer	2	1.6
13	Urinary Tract Infections	2	1.6
14	Parkinson's Disease	2	1.6
15	Carcinoma	2	1.6
16	Acute Kidney Injury	2	1.6
17	CRF	1	0.1
18	COPD	1	0.1
19	Liver Cirrhosis	1	0.1
20	CVA	1	0.1
21	Others	9	6.9

The study results on major clinical conditions revealed that 27% were affected with Diabetes mellitus followed by 23% with hypertension, coronary heart disease 9.3%, renal disorders 4.3% and 6.9% with other clinical conditions.

TABLE NO.5

THERAPEUTIC CATEGORY OF DRUGS PRESCRIBED

(n= 1058)

S.No	Categories of drugs	No. of drugs	Percentage (%)
1	Antihypertensives	203	15.21
2	Antibiotics	126	11.91
3	Antidiabetics	93	8.70
4	Proton Pump Inhibitors	87	8.22
5	NSAIDs	64	6.05
6	Anti-anxiety	59	5.51
7	Antiemetics	58	5.48
8	Analgesics	45	4.25
9	Anticonvulsants	40	3.78
10	Potassium Supplements	30	2.83
11	HMG-CoA Reductase Inhibitors	26	2.46
12	Corticosteroids	26	2.46
13	Antacids	25	2.36
14	Anticoagulants	25	2.36
15	CVS agents	21	0.85
16	Neuromuscular Blockers	9	0.50
17	Antianginals	9	0.50
18	Antidotes	6	0.47
19	Thrombolytics	6	0.47
20	Anticholinergics	5	0.19
21	Others	127	12.1

The major categories of drugs in the prescriptions were anti-hypertensives (15.21%), antibiotics (11.91%), anti-diabetic drugs (8.70%), proton pump inhibitors (8.22%), NSAIDs (6.05%) and others.

TABLE NO.6

ANTI-HYPERTENSIVES PRESCRIBED

(n= 203)

Category	Number	Percentage (%)
Diuretics	122	60.09
ACE inhibitors	22	10.84
Beta blockers	20	9.85
Calcium channel blockers	13	6.4
Angiotensin receptor blockers	12	5.9
α+β blockers	8	3.9
Centrally acting drugs	6	2.9

The study reports that 60.09% of diuretics were used in the study population, ACE inhibitors (10.84%), beta blockers (9.85%), calcium channel blockers (6.4%), angiotensin receptor blockers (5.9%), α+β blockers (3.9%), centrally acting drugs (2.9%).

TABLE NO.7

CATEGORY OF DIURETICS PRESCRIBED

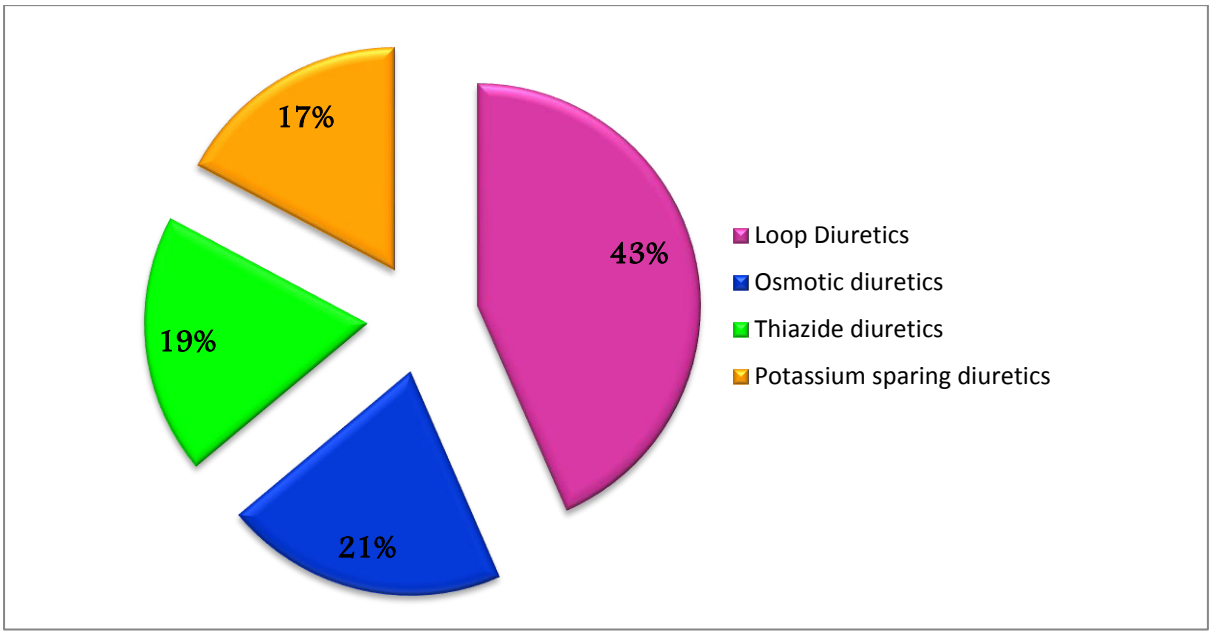
(n=122)

S.No	Category	Number	Percentage (%)
1	Loop diuretics	53	43.44
2	Osmotic diuretics	25	20.49
3	Thiazide diuretics	23	18.85
4	Potassium sparing diuretics	21	17.21

FIGURE NO.4

CATEGORY OF DIURETICS PRESCRIBED

(n=122)



The study reveals that major diuretics used in the study population are loop diuretics (43.44%), osmotic diuretics (20.49%), thiazide diuretics (18.85%) and potassium sparing diuretics (17.21%).

TABLE NO.8

NUMBER OF DIURETICS PRESCRIBED

(n=122)

S.No	Drugs	Category	No. of drugs	Percentage(%)
	Monotherapy			
1	Frusemide	Loop diuretic	28	22.95
2	Torsemide	Loop diuretic	25	20.49
3	Spironolactone	Potassium sparing diuretic	25	20.49
4	Mannitol	Osmotic diuretic	14	11.48
5	Hydrochlorthiazide	Thiazide diuretic	13	10.66
6	Metolazone	Thiazide diuretic	3	2.5
	Combination therapy			
7	Torsemide+ Spironolactone	Loop diuretic+ Potassium sparing diuretic	8	6.56
8	Telmisartan+ Hydrochlorthoazide	ARBs+ Potassium sparing diuretic	7	5.74

The study reports that the prescribed diuretics were frusemide (22.95%), torsemide (20.49%), spironolactone (20.49%), mannitol (11.48%), hydrochlorthiazide (10.66%), metolazone (2.5%) and combination therapy of diuretics include torsemide and spironolactone (6.56%), telmisartan and hydrochlorthiazide (5.74%).

TABLE NO. 9

ELECTROLYTE DISORDERS

(n=164)

S.No	Electrolyte Disorders	Number	Percentage (%)
1	Hyperchloremia	51	31.09
2	Hyperbicarbonatremia	38	1.83
3	Hypokalemia	23	14.02
4	Hypernatremia	14	8.53
5	Hypochloremia	14	8.53
6	Hyponatremia	8	4.84
7	Hyperphosphatemia	5	3.04
8	Hypercalcemia	4	2.43
9	Hypobicarbonatremia	3	2.21
10	Hyperkalemia	2	1.21
11	Hypocalcemia	1	0.06
12	Hypermagnesemia	1	0.06

The study reports that 31.09% of patients had hyperchloremia, 1.83% with hyperbicarbonatemia, 14.02% with hypokalemia,8.53% with hypernatremia and hypochloremia, 4.84% with hyponatremia, 3.04% with hyperphosphatemia, 2.43% with hypercalcemia, 2.21% with hypobicarbonatemia, 1.21% with hyperkalemia, 0.06% with hypocalcemia and hypermagnesemia.

TABLE NO. 10

DRUG INTERACTIONS

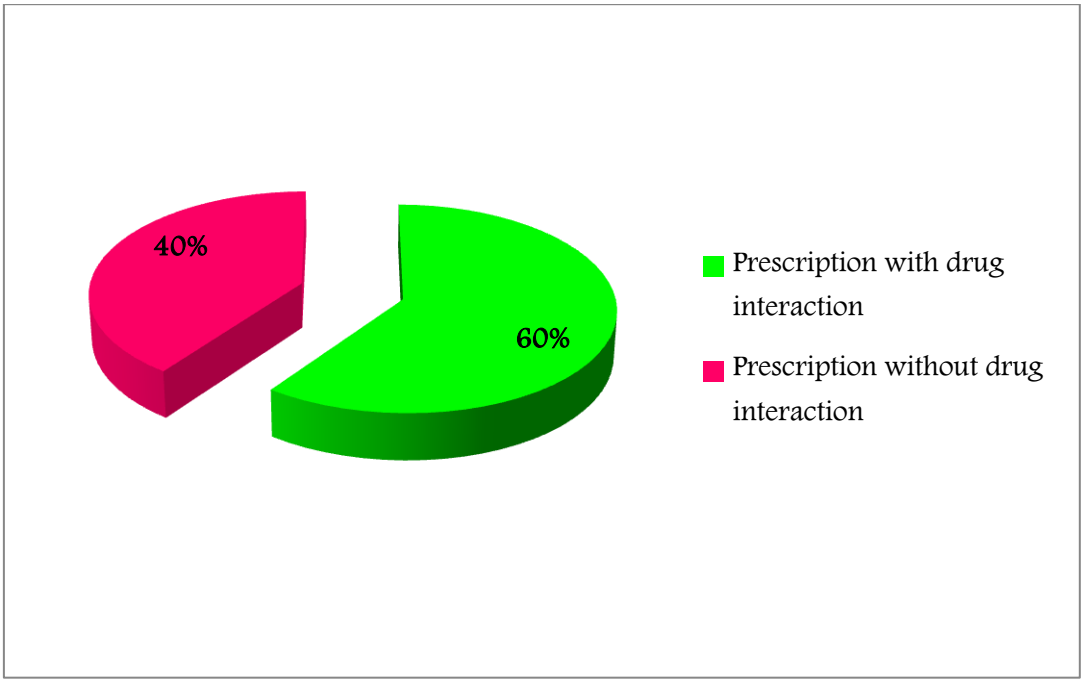
(n=100)

Prescription Screened	No. of Prescription	Percentage (%)
Prescription with drug interaction	60	60
Prescription without drug interaction	40	40

FIGURE NO.10

DRUG INTERACTIONS

(n=100)



Out of 100 prescriptions, 60% of the prescription had drug interaction and 40% of the prescription had no drug interactions.

TABLE NO.11

SEVERITY OF DRUG INTERACTIONS

(with diuretics)

(n= 22)

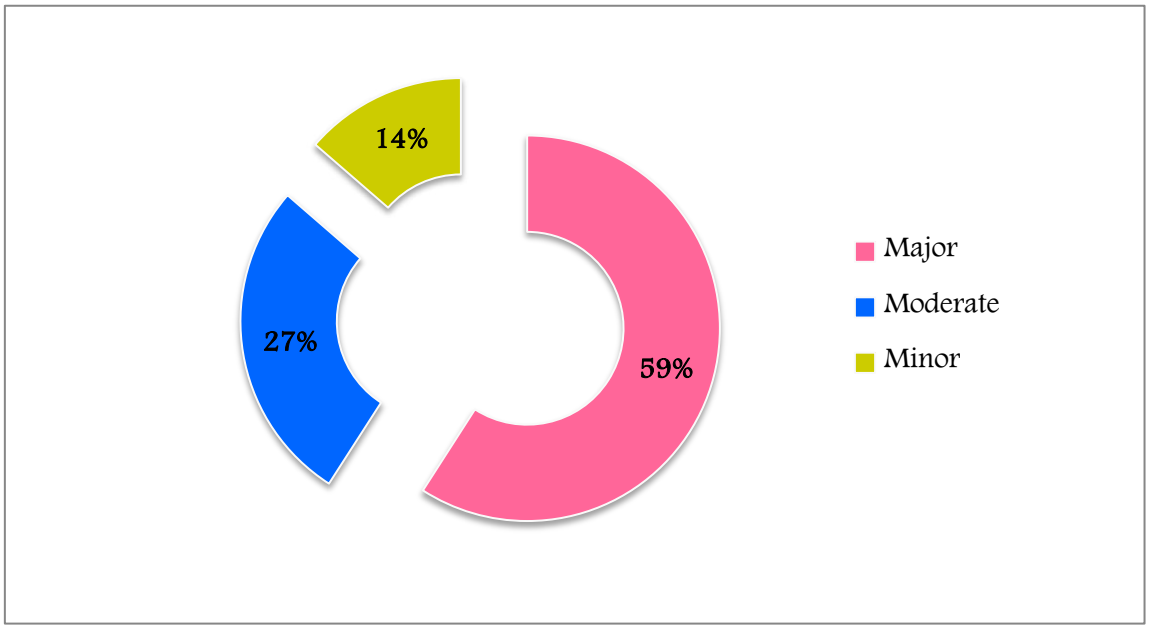
Severity	Number of Interactions	Percentage (%)
Major	13	59.09
Moderate	6	27.27
Minor	3	13.63

FIGURE NO.11

SEVERITY OF DRUG INTERACTIONS

(with diuretics)

(n= 22)



The study states that 59.09 % were major drug interactions, 27.27% were moderate and 13.63% were minor drug interactions.

DISCUSSION

The current study revealed that the number of males in study population was high compared to females. A similar result was published in the study done by ***Anusha N et al (2014)***[4] reported that there were more number of male patients than the female patients in the study group. By analyzing the social history of the patients, it was found that most of them were smokers and alcoholics. Age distribution results shows that majority of patients were between the age group of 51-65 years. Major diagnosis observed in the current study were diabetes mellitus, systemic hypertension, coronary artery disease and renal disorders. Results of age characterization and diagnosis can be compared with the study conducted by ***Kurnal C Solanki et al (2013)***[6] which states that maximum patients belonged to age group of 51-65 years and diabetes mellitus was the most common diagnosis with hypertension.

On evaluation of prescriptions, commonly prescribed category of drugs were antihypertensives, antibiotics, anti-diabetics and gastrointestinal drugs. Antihypertensives account for major use followed by antibiotics, anti-diabetics and proton pump inhibitors. Majority of the anti hypertensives used in the present study were diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers and calcium channel blockers. A similar study was performed by ***Jainaf Nachiya et al (2015)***[27] states that anti-hypertensives, angiotensin converting enzyme inhibitors and calcium channel blockers were frequently used for the treatment. Among diuretics prescribed, it was observed that loop diuretics accounts for the maximum use followed by thiazide, osmotic and potassium sparing diuretics. This result can be compared with the study conducted by ***Aram V et al (2009)***[38]which states that most commonly prescribed diuretics were loop, thiazide and potassium sparing.

Diuretics used as monotherapy in the study were frusemide, torsemide, spironolactone, mannitol, hydrochlorthiazide and metalazone. Combination therapy prescribed were telmisartan + hydrochlorthiazide and torsemide +spironolactone. Hypokalemia and hypernatremia accounts for majority of diuretic induced electrolyte disturbances in the study population. Other electrolyte disturbances observed in study

include hyperkalemia, hyponatremia, hypochloremia, hyperchloremia, hyperphosphotaemia, hypophosphatemia, hypomagnesemia, hypermagnesemia, hyperbicarbonatremia, hypobicarbonatremia, hypercalcemia and hypocalcemia. A similar study conducted by ***Spyridon Arampatzis et al (2013)***[30] have concluded that hyponatremia, hypernatremia and hyperkalemia were observed in patients receiving diuretic therapy.The study revealed that 60% of the prescriptions had drug interactions, out of which more than 50% were found to have major severity. The major severity was observed between spironolactone and frusemide.

CONCLUSION

Through the current study, we could assess the drug utilization pattern of diuretics in intensive care unit and general medicine department. The study report shows male population was higher compared to females. Diabetes mellitus and systemic hypertension were the predominal diagnosis in intensive care unit and general medicine department. Angiotensin converting enzyme inhibitors and diuretics were the most frequently utilized drugs in the study. Among diuretics, frusemide, spironolactone and mannitol were highly utilized in intensive care unit and general medicine department. Since diuretic induced electrolyte imbalance were observed during the current study, the clinical pharmacist can be effectively employed to monitor the electrolyte levels to reduce the adverse effects.

Pharmacist can play an important role to avoid adverse effects associated with diuretics by discussing with the prescriber about drugs and their safety, alternatives, so that an appropriate decision is made about the patient's therapeutic plan. The current study assessed the major drug interactions which were found to be highly significant. Identifying and monitoring drug interactions has a significant part in forming a standard therapeutic plan will reduce the occurrence of adverse events.

Understanding these disturbances can improve the patient care, be cost-effective, prevent complications from primary disease and ultimately reduce mortality and morbidity[30].

FUTURE OUTLOOK

The present study can help to adopt a continuous electrolyte monitoring system in hospital to minimize the complications of electrolyte disorders. Health care professionals can stand as a team to know the importance of electrolyte monitoring in reducing the adverse effects associated with drugs prescribed. The study can be extended in large group of patients to analyze the electrolyte disorders. therapeutic guidelines can be prepared for selecting the appropriate anti-hypertensives and diuretics for a better patient care. Educating the patients about lifestyle modification of hypertension shall minimize the use of diuretics in hypertensive patients. Pharmacoeconomic studies on diuretics can be used for the improvement of medical care and cost containment and are useful for measuring or comparing the economic impact of drug use in specific population groups by identifying adherence to guidelines in the current use of medicines, it is possible to reduce drugs expenditure and improve the allocation of the limited resources available, when the chosen drugs are not usually the most cost effective.

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